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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/509,249	09/28/2004	Shunichi Kuroda	12480-000067/US	4499

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EXAMINER	
PENG, BO	
ART UNIT	PAPER NUMBER
1648	
MAIL DATE	DELIVERY MODE
09/29/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/509,249	KURODA ET AL.	
	Examiner	Art Unit	
	BO PENG	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 August 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-7,9,14,15 and 29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 5-7, 9, 14, 15 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/5/10*
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 5, 2010, has been entered.

2. Claims 2-4, 8, 10-13, and 16-28 have been cancelled. New Claim 29 has been added. Accordingly, Claims 1, 5-7, 9, 14, 15 and 29 are pending and are considered in this Office action.

Interview with Applicant's Representative

3. An interview was conducted between the examiner and Applicant's representative Erin Hoffman on September 20, and 21, 2010. See Interview Summary mailed on September 23, 2010. On September 24, attorney Hoffman informed the examiner that Applicant needs more time to work out the terminal disclaimer.

Title

4. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

Claim Objections

5. **(Prior objection-withdrawn)** The objection to Claim 1 for minor informalities is withdrawn in view of the amendment to the claim. The objection to Claims 6 and 25 for being duplicates thereof, is withdrawn in view of the cancellation of Claim 25.

6. **(New objection)** Claim 1 recites: "...an antibody against a specific cell or specific tissue,.." However, an antibody is known to be capable of targeting against an antigen, but not "against a specific cell or specific tissue". Appropriate correction is required.

Claim Rejections - 35 USC 112, second paragraph

7. The following is a quotation of the second paragraph of 35 USC 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. **(Prior rejection-withdrawn)** The rejection of Claims 1, 5-7, 9, 14 and 15 under 35 USC 112, second paragraph, for failing to define the limitation "cancer specific antibody", **is withdrawn** in view of the amendment to Claim 1. Claim 1 has been amended to eliminate the term "cancer specific antibody".

Claim Rejections - 35 USC 112, first paragraph

9. The following is a quotation of the first paragraph of 35 USC 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. **(Prior rejection-maintained)** The rejection of Claims 1-3, 5-9, 14-16, 22, 24 and 25 under 35 USC 112, first paragraph, as failing to comply with the enablement requirement, **is maintained** for the reasons of record.

In response to Applicant's argument:

11. Applicants submit that the Examiner does not seem to sufficiently take into consideration the previously submitted Declarations as the term "substance carrier" has been clearly distinguished from the term "drug". As additional evidence, Applicants attach a Declaration executed by Mr. Kuroda, which gives additional evidence of how a "substance carrier" can be implemented.

12. Applicants' argument is considered, but not persuasive. MPEP 2111 recites: "During patent examination, the pending claims must be "given their broadest reasonable interpretation consistent with the specification." >The Federal Circuit's en banc decision in Phillips v. AWH Corp., 415 F.3d 1303, 75 USPQ2d 1321 (Fed. Cir. 2005). Applicant always has the opportunity to amend the claims during prosecution, and broad interpretation by the examiner reduces the possibility that the claim, once issued, will be interpreted more broadly than is justified. In re Prater, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-51 (CCPA1969). In the present case,
although the claims have been amended from prior "drug" to "substance carrier", the specification indicates that the term "substance carrier" is equivalent to "drug" in this application; see e.g. Para 3, p. 16; and Para 2, p. 17. Therefore, according to the specification, the term "substance carrier" still reads on "drug". However, the specification has not taught one of ordinary skill in the art how to use HBsAg L protein for treating un-defined diseases; see discussion in Para 12 and 13 of the Office action

dated June 1, 2010. Thus, Applicant's argument is not sufficient to overcome the rejection.

13. However, According to MPEP 2111 cited above, "Applicant always has the opportunity to amend the claims during prosecution, and broad interpretation by the examiner reduces the possibility that the claim, once issued, will be interpreted more broadly than is justified". If the claims are amended to be directed to "A hollow nanoparticle for delivering a substance to a cell...", which is supported by the specification Para [0072], this would overcome the rejection.

Claim Rejections - 35 USC 103

14. The following is a quotation of 35 USC 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 USC 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of their obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 USC 103(c) and potential 35 USC 102(e), (f) or (g) prior art under 35 USC 103(a).

15. **(Prior rejection-maintained-extended)** Claims 1, 3, 5-7, 9, 14, 22, 24 and 25 are rejected under 35 USC 103(a) as being unpatentable over Kuroda (WO 01/64930, which is PCT/JP01/00926, International publication date: September 7, 2001, cited in IDS. The

US2003/0092069, which is the National stage of PCT/JP01/00926, is cited as the English translation of WO 01/64930) and Ojala K, *et al*. (Biochem Biophys Res Commun. 2001;284(3):777-84), **is maintained** and **extended** to new Claim 29 for the reason of record.

In response to Applicant's arguments:

13. Applicant argues **(1)** that Ojala teach a viral particle comprising a ZZ Tag, but not a particle comprising ZZ tag and an antibody, as shown on p. 780. As such, neither Kuroda, Ojala nor the combination thereof teaches or suggests "a substance carrier comprising hollow nanoparticles of a particle-forming protein, the hollow nanoparticles displaying an antibody against a specific cell or specific tissue, the antibody being displayed on the surface of the nanoparticles by binding to a ZZ tag fused with the particle-forming protein" as recited in independent Claim 1. **(2)** the Examiner fails to point out (nor can Applicants Find) where Kuroda, Ojala or the combination thereof teaches "encapsulating a substance to be transferred into a cell" as recited in independent Claim 1. The Applicants, therefore, respectfully request that the rejection to Claim 1 be withdrawn.

14. In response to applicant's argument (1), the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). In the present case, Claim 1 requires: "..., the hollow nanoparticles displaying an antibody against a specific cell or specific tissue,... the antibody being displayed on the surface of the nanoparticles by binding to a ZZ tag fused with the particle-forming protein...". Ojala teaches a baculovirus particle comprising ZZ tag, which targets BHK cells *via* binding of an appropriate IgG antibody. In view of this teaching, one of ordinary skill in the art would readily understand that a

particle comprising a ZZ tag and an antibody to a molecule on a cell can be used to target the cell of interested as shown by Ojala. It is within one of ordinary skill in the art to conjugate an antibody to ZZ tag as shown by Ojala. Thus, the claimed invention as whole is obvious to one of ordinary skill in the art.

15. In response to Applicants argument (2), Ojala teaches encapsulating an EGFP gene (a substance) in Baculovirus particle, see Para 1, left col. p. 779 and Fig 1B. Ojala also shows EGFP was transferred into BHK cells, see bridging Para between pp. 781-782; and Fig.6. Also see Para 34, the previous office action. Since the Office action has clearly indicted how Ojala teaches the limitation of "encapsulating a substance to be transferred into a cell", Applicant's argument (2) is not convincing.

16. Since applicant has not presented any compelling reasons or evidence to overcome this rejection, the rejection is therefore maintained.

17. **(New rejection-maintained) The rejection of** Claim 15 under 35 USC 103(a) as being unpatentable over Kuroda (WO 01/64930) and Ojala , as applied to Claim 1 and 14 above, and further in view of Rosenfeld, **is maintained** for the reason of record.

18. Applicant argues that the Examiner has failed to show how Rosenfeld remedies the deficiencies of Kuroda and Ojala with respect to independent Claim 1. Thus, Claim 15 is patentable over Rosenfeld and Kuroda and Ojala for the reasons set forth above with respect to independent Claim 1.

19. This argument is not relevant. The combined teaching of Kurola and Ojala has taught and suggested each and every limitation of Claim 1. The cited Rosenfeld teaches the limitation of Claim 15, as indicated in Para 39 of the previous office action. Thus,

Applicant's argument is not relevant.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

20. **(Prior rejection-moot)** The rejection of Claims 1-3, 5-9, 14-16, 22, 24 and 25 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 1-3, 6, 8 and 9 of application **11/987,476, is moot** in view of the amendment of '476.

21. **(New rejection)** Claims 1, 5-7, 9, 14, 15 and 29 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 1-3 of US Pat. **7,597,905**. Although the conflicting claims are not identical, Claims 1, 5-7, 9, 14, 15 and 29 are not patentably distinct from Claims 1-3 of '905 because the examined

application claims would have been obvious over the reference claim(s), in view of Kuroda (WO 01/64930) and Ojala, *et al.* (Biochem Biophys Res Commun. 2001; 284(3):777-84).

22. Claims 1-3 are directed to a transporter for transferring a substance into target cells or tissues, comprising a hollow nanoparticle obtained by expressing a hepatitis B virus surface antigen protein or mutant thereof capable of forming a particle in a eukaryotic cell, and incorporated therein is a substance to be introduced into the target cell or tissues, wherein the substance is selected from the group consisting of genes, oligonucleotides, natural or synthetic proteins peptides and drugs, wherein the hepatitis B virus surface antigen protein is a hepatitis B virus surface antigen L-protein, wherein the amino acid at positions 129 and 145 of the S-protein site are both substituted with arginine. However, Claims 1-3 do not teach the HBV surface antigen comprising a ZZ tag for displaying an antibody.

23. Kuroda (WO 01/64930) teaches hollow nanoparticles composed of HBsAg L protein a biorecognition molecule to introduce a substance (gene, protein, compound, etc.) into the target cells or tissue, wherein the biorecognition molecule on the hollow nanoparticles is an antibody; see the English translation of Abstract (WO 01/64930), and see also see Para [0009]-[0016] and the claims of US2003/0092069.

24. Ojala teaches use of baculovirus (nanoparticle) comprising ZZ tag to bind IgG antibody on BHK cells. In addition, the baculovirus vectors were engineered to incorporate a reporter gene encoding the enhanced green fluorescent protein (EGFP). Ojala teaches that such viral particles displaying specific ZZ ligand binding moieties have raised an increasing interest in the area of targeted gene therapy, see e.g. Abstract.

25. It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the HBsAg L protein nanoparticle of Claims 1-3 of US Pat. **7,597,905** by incorporating ZZ tag in order to display an antibody as suggested by Kuroda and as taught by Ojala. The skilled artisan would have been motivated to do so, and would have a reasonable expectation of success, given the knowledge that HBsAg L protein comprising Ab can be used as a drug delivery system for delivering a nucleic acid drug, as taught by Claims 1-3 of US Pat. **7,597,905** and Kuroda and also given the knowledge that ZZ tag-antibody can be used to target specific cells, as taught by Ojala. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Remarks

26. No claims are allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bo Peng, Ph.D. whose telephone number is 571-272-5542. The examiner can normally be reached on Tu-F, 8:30-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Zachariah Lucas can be reached on 571-272-0905. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/BO PENG/
Primary Examiner, Art Unit 1648